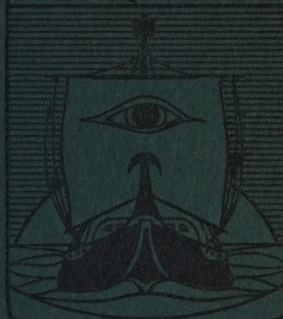


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Malaria

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in Simple Tertian Malaria?

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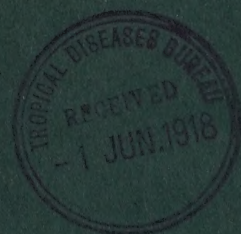
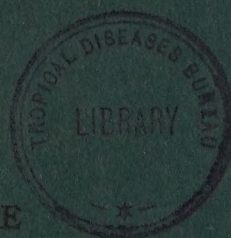
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STUDIES IN THE TREATMENT OF MALARIA

XII. AT WHAT TIME AFTER CESSATION OF QUININE TREATMENT DO RELAPSES OCCUR IN SIMPLE TERTIAN MALARIA?

BY

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Undertaken at the request of the War Office

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The primary object of this analysis is to determine the shortest period after cessation of treatment for which it is necessary to keep under observation a case of simple tertian malaria, so that the probability of a relapse occurring after discharge from hospital is reasonably small. With this in view, we have analysed the time incidence of relapses in four hundred and five cases treated by us in various ways as recorded in previous papers. Almost all these cases were adult males infected in Macedonia six to twelve months previously, and all had had more or less quinine during that period.

We consider parasitic relapses only, as we know nothing of the nature of febrile paroxysms unassociated with parasites in the peripheral blood.

The data on which this paper is based are given in Tables I to III. Tables I and II contain the results of those treatments where quinine was administered either on a single occasion or on two

Relapse time after administration of quinine on either one or two consecutive days only

Observation period after cessation of treatment in 3-day periods	Treatments							
	Quinine bihydrochloride grains 5 orally on each of two consecutive days		Quinine sulphate grains 5 orally on each of two consecutive days		Quinine sulphate grains 10 orally on each of two consecutive days		Quinine sulphate grains 15 orally on each of two consecutive days	
	Cases treated : 17 Relapses : 17		Cases treated : 8 Relapses : 7		Cases treated : 10 Relapses : 10		Cases treated : 14 Relapses : 14	
	Non-relapse cases still in hospital at beginning of each 3-day period	Cases relapsing during each 3-day period	Non-relapse cases still in hospital at beginning of each 3-day period	Cases relapsing during each 3-day period	Non-relapse cases still in hospital at beginning of each 3-day period	Cases relapsing during each 3-day period	Non-relapse cases still in hospital at beginning of each 3-day period	Cases relapsing during each 3-day period
1-3	17	1	8	0	10	0	14	0
4-6	16	1	8	3	10	0	14	0
7-9	15	1	5	1	10	0	14	4
10-12	14	8	4	2	10	6	10	5
13-15	6	6	2	0	4	2	5	3
16-18	0	0	2	1	2	2	2	1
19-21	...	...	1	0	0	0	1	0
22-24	...	...	1	0	...	...	1	1
25-27	...	...	1	0	...	...	0	0
28-30	...	...	1	0	...	...	...	...
31-33	...	...	1	0	...	...	...	...
34-36	...	...	1	0	...	...	...	...
37-39	...	...	1	0	...	...	...	...
40-42	...	...	1	0	...	...	...	...
43-45	...	...	1	0	...	...	...	...
46-48	...	...	1	0	...	...	...	...
49-51	...	...	1	0	...	...	...	...
52-54	...	...	1	0	...	...	...	...
55-57	...	...	1	0	...	...	...	...
58-60	...	...	1	0	...	...	...	...
61-63	...	...	0	0	...	...	...	...

in those series where no curative effect was obtained.

1-7							
Quinine sulphate grains 30 orally on each of two consecutive days		Quinine bihydrochloride grains 15 intramuscularly on each of two consecutive days		Quinine bihydrochloride grains 10-15 intravenously (single injection)		Summary of results of the seven treatments	
Cases treated : 14 Relapses : 14		Cases treated : 20 Relapses : 19		Cases treated : 6 Relapses : 6		Total cases treated : 89 Total relapses : 87	
Non-relapse cases still in hospital at beginning of each 3-day period	Cases relapsing during each 3-day period	Non-relapse cases still in hospital at beginning of each 3-day period	Cases relapsing during each 3-day period	Non-relapse cases still in hospital at beginning of each 3-day period	Cases relapsing during each 3-day period	Total non-relapse cases still in hospital at beginning of each 3-day period	Total cases relapsing during each 3-day period
14	0	20	0	6	0	89	1
14	0	20	0	6	1	88	5
14	2	20	3	5	2	83	13
12	5	17	5	3	1	70	32
7	5	12	10	2	2	38	28
2	0	2	1	0	0	10	5
2	2	1	0	...	...	5	2
0	0	1	0	...	...	3	1
...	...	1	0	...	...	2	0
...	...	1	0	...	...	2	0
...	...	1	0	...	...	2	0
...	...	1	0	...	...	2	0
...	...	1	0	...	...	2	0
...	...	1	0	...	...	2	0
...	...	1	0	...	...	2	0
...	...	1	0	...	...	2	0
...	...	1	0	...	...	2	0
...	...	1	0	...	...	2	0
...	...	1	0	...	...	2	0
...	...	1	0	...	...	2	0
...	...	1	0	...	...	2	0
...	...	0	0	...	...	0	0

Relapse time after administration of quinine on either one or two consecutive days

Observation period after cessation of treatment in 3-day periods	Treatments					
	Quinine sulphate grains 45 orally on each of two consecutive days		Quinine sulphate grains 60 orally on each of two consecutive days		Quinine sulphate grains 90 orally on each of two consecutive days	
	Cases treated : 12 Relapses : 9		Cases treated : 12 Relapses : 7		Cases treated : 76 Relapses : 29	
	Non-relapse cases still in hospital at beginning of each 3-day period	Cases relapsing during each 3-day period	Non-relapse cases still in hospital at beginning of each 3-day period	Cases relapsing during each 3-day period	Non-relapse cases still in hospital at beginning of each 3-day period	Cases relapsing during each 3-day period
1-3	12	0	12	0	76	0
4-6	12	0	12	0	76	0
7-9	12	0	12	0	76	0
10-12	12	0	12	1	76	0
13-15	12	5	11	1	76	3
16-18	7	1	10	3	73	7
19-21	6	2	7	1	66	8
22-24	4	0	6	0	58	5
25-27	4	1	6	1	53	2
28-30	3	0	5	0	51	0
31-33	3	0	5	0	51	1
34-36	3	0	5	0	50	1
37-39	3	0	5	0	49	1
40-42	3	0	5	0	48	0
43-45	3	0	5	0	48	0
46-48	3	0	5	0	48	0
49-51	3	0	5	0	48	0
52-54	0	0	5	0	48	0
55-57	...	...	5	0	46	1
58-60	...	...	5	0	44	0
61-63	...	...	5	0	42	0
64-66	...	...	0	0	39	0
67-69	...	...	...	...	28	0
70-72	...	...	...	...	25	0
73-75	...	...	...	...	23	0
76-78	...	...	...	...	17	0
79-81	...	...	...	...	13	0
82-84	...	...	...	...	9	0
85-87	...	...	...	...	8	0
88-90	...	...	...	...	7	0

II

only in those series where some curative effect was obtained.

8-12

Quinine sulphate grains 120 orally on each of two consecutive days		Quinine alkaloid grains 15-60 <i>intravenously</i> (either one or two injections)		Summary of results of the five treatments	
Cases treated : 15 Relapses : 9		Cases treated : 38 Relapses : 31		Total cases treated : 153 Total relapses : 85	
Non- relapse cases still in hospital at <i>beginning</i> of each 3-day period	Cases relapsing <i>during</i> each 3-day period	Non- relapse cases still in hospital at <i>beginning</i> of each 3-day period	Cases relapsing <i>during</i> each 3-day period	Total non- relapse cases still in hospital at <i>beginning</i> of each 3-day period	Total cases relapsing <i>during</i> each 3-day period
15	0	38	0	153	0
15	0	38	0	153	0
15	0	38	0	153	0
15	2	38	1	153	4
13	4	37	9	149	22
9	2	28	9	127	22
7	0	19	4	105	15
7	1	15	5	90	11
6	0	10	3	79	7
6	0	7	0	72	0
6	0	7	0	72	1
6	0	7	0	71	1
6	0	7	0	70	1
6	0	7	0	69	0
6	0	7	0	69	0
6	0	7	0	69	0
6	0	7	0	69	0
6	0	7	0	66	0
6	0	7	0	64	1
6	0	7	0	62	0
5	0	0	0	52	0
4	0	...	...	43	0
3	0	...	...	31	0
3	0	...	...	28	0
2	0	...	...	25	0
1	0	...	...	18	0
1	0	...	...	14	0
0	0	...	...	9	0
...	...	...	...	8	0
...	...	...	...	7	0

Relapse time after prolonged administration of quinine by

Observation period after cessation of treatment in 3-day periods	Continuous									
	Quinine sulphate grains 20 orally daily for 14-15 weeks		Quinine sulphate grains 30 orally daily for 5-18 weeks		Quinine sulphate grains 30 orally daily for 8 weeks		Quinine sulphate grains 30 orally daily for 3 weeks grains 45 orally daily for 1 week		Quinine sulphate grains 45 orally daily for 3-8 weeks	
	Cases treated : 5 Relapses : 3		Cases treated : 14 Relapses : 10		Cases treated : 29 Relapses : 24		Cases treated : 22 Relapses : 17		Cases treated : 19 Relapses : 7	
	Non-relapse cases still in hospital at beginning of each 3-day period	Cases relapsing during each 3-day period	Non-relapse cases still in hospital at beginning of each 3-day period	Cases relapsing during each 3-day period	Non-relapse cases still in hospital at beginning of each 3-day period	Cases relapsing during each 3-day period	Non-relapse cases still in hospital at beginning of each 3-day period	Cases relapsing during each 3-day period	Non-relapse cases still in hospital at beginning of each 3-day period	Cases relapsing during each 3-day period
1-3	5	1	14	1	29	0	22	2	19	0
4-6	4	0	13	0	29	4	20	1	19	0
7-9	4	2	13	4	25	4	19	3	19	1
10-12	2	0	9	0	21	8	16	2	18	2
13-15	2	0	9	1	13	1	14	4	16	1
16-18	2	0	8	0	12	1	10	3	15	1
19-21	2	0	8	1	11	1	7	0	14	0
22-24	2	0	7	0	10	0	7	0	14	0
25-27	2	0	7	0	10	0	7	0	14	1
28-30	2	0	7	0	8	3	7	0	13	0
31-33	2	0	7	2	5	1	7	0	12	0
34-36	1	0	5	0	4	1	6	0	11	0
37-39	1	0	5	0	3	0	6	1	10	1
40-42	1	0	5	0	3	0	5	0	9	0
43-45	1	0	5	0	3	0	5	0	9	0
46-48	1	0	5	1	2	0	5	0	9	0
49-51	1	0	4	0	0	0	5	0	9	0
52-54	1	0	4	0	...	...	5	0	9	0
55-57	1	0	4	0	...	...	5	0	9	0
58-60	1	0	4	0	...	...	5	1	9	0
61-63	1	0	4	0	...	...	4	0	5	0
64-66	1	0	1	0	...	...	1	0	3	0
67-69	1	0	1	0	...	...	1	0	2	0
70-72	1	0	1	0	...	...	1	0	2	0
73-75	1	0	0	0	...	...	1	0	1	0
76-78	1	0	...	...	...	...	1	0	1	0
79-81	0	0	...	...	...	...	1	0	1	0
82-84	...	...	...	...	...	...	1	0	1	0
85-87	...	...	...	...	...	...	1	0	0	0
88-90	...	...	...	...	...	...	1	0	...	...

consecutive days only, and are therefore comparable. In Table I are recorded those treatments in which practically no curative effect was obtained (eighty-nine cases, eighty-seven relapses), whilst in Table II are recorded those treatments in which a definite curative effect was obtained (one hundred and fifty-three cases, eighty-five relapses). In Table III are grouped together the results obtained by us with various prolonged treatments, *continuous* or *interrupted*. In most of these some curative effect was obtained (one hundred and sixty-three cases, ninety-six relapses).

One of the first questions that present themselves is whether the time incidence of relapses varies at all with the nature of the treatment employed; for example, do relapses occur more quickly after a small dose of quinine than after a large dose?

Owing to the relatively small number of cases in many of the Series of treatments 1 to 21, it is not practicable to compare the time incidence of relapses in each of the individual series. By arranging the series in groups as has been done in Tables I to III, numbers are obtained which are sufficiently large to permit of comparison. In order to decide whether the time incidence of relapses is dependent on the nature of the treatment

TABLE IV.

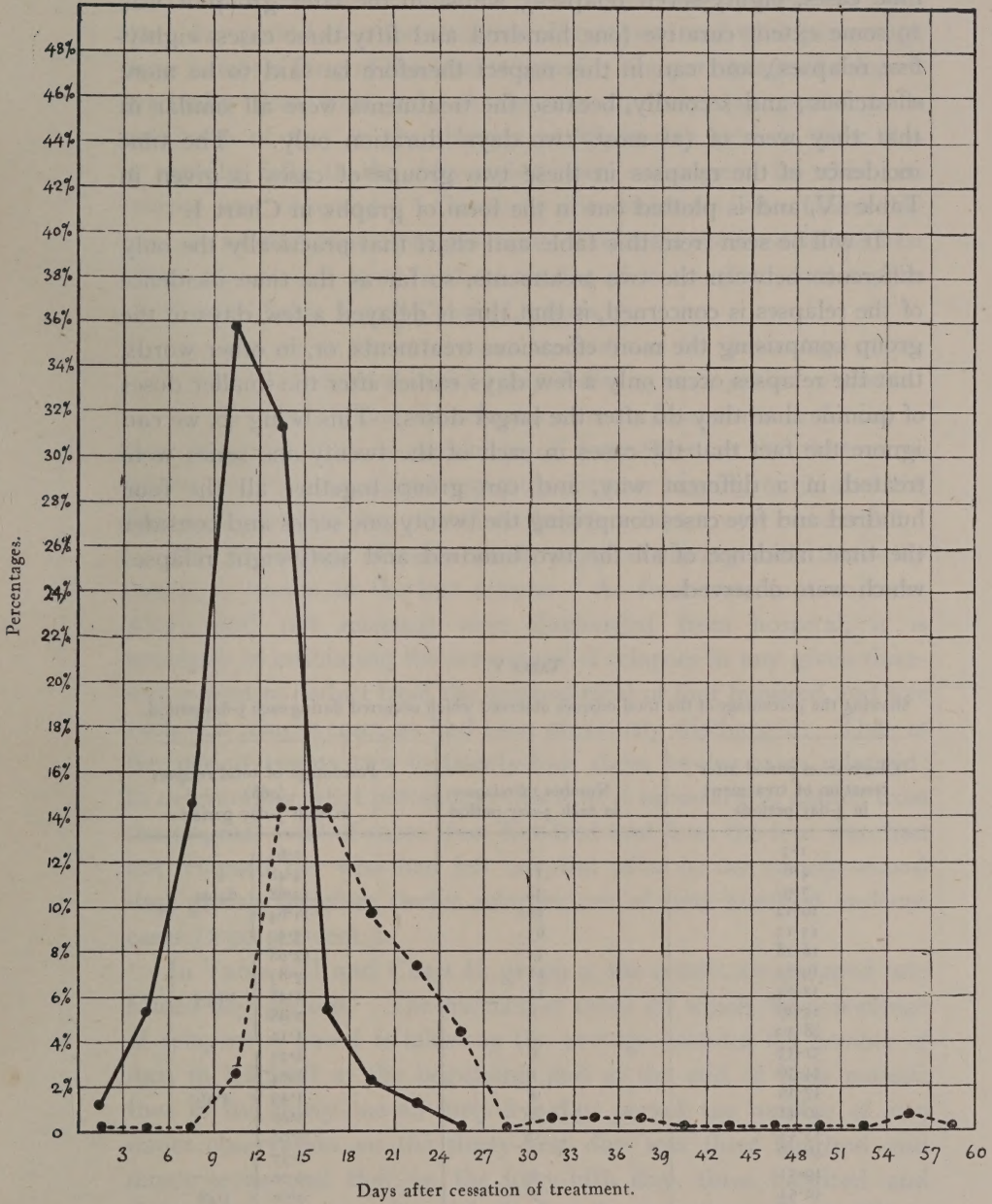
Comparing the percentage of cases treated which relapsed during each 3-day period after cessation of treatment in Series 1-7 (Table I) with those in Series 8-12 (Table II).

Observation period after cessation of treatment in 3-day periods	Number of cases treated on which the percentage of relapses is calculated		Number of cases which relapse during each 3-day period		Percentage of cases treated which relapse during each 3-day period	
	Series 1-7	Series 8-12	Series 1-7	Series 8-12	Series 1-7	Series 8-12
1-3	89	153	1	0	1.12	0.00
4-6	89	153	5	0	5.60	0.00
7-9	89	153	13	0	14.60	0.00
10-12	89	153	32	4	35.95	2.61
13-15	89	153	28	22	31.44	14.45
16-18	89	153	5	22	5.60	14.45
19-21	89	153	2	15	2.24	9.80
22-24	89	153	1	11	1.12	7.18
25-27	89	153	0	7	0.00	4.57
28-30	...	153	...	0	...	0.00
31-33	...	153	...	1	...	0.65
34-36	...	153	...	1	...	0.65
37-39	...	153	...	1	...	0.65
40-42	...	153	...	0	...	0.00
43-45	...	153	...	0	...	0.00
46-48	...	153	...	0	...	0.00
49-51	...	153	...	0	...	0.00
52-54	...	150	...	0	...	0.00
55-57	...	148	...	1	...	0.67
58-60	...	147	...	0	...	0.00

CHART I.

Percentage of cases treated which relapse during each 3-day period.

Series 1-7 ———; Series 8-12 - - -



employed, we have selected for comparison the results obtained in Series 1 to 7 (Table I) and those in Series 8 to 12 (Table II); firstly, because treatment in the earlier series was purely palliative (eighty-nine cases, eighty-seven relapses), whilst in the later group it was to some extent curative (one hundred and fifty-three cases, eighty-five relapses), and can in this respect therefore be said to be more efficacious; and secondly, because the treatments were all similar in that they were of (at most) two days' duration only. The time incidence of the relapses in these two groups of cases is given in Table IV, and is plotted out in the form of graphs in Chart I.

It will be seen from this table and chart that practically the only difference between the two treatments, so far as the time incidence of the relapses is concerned, is that this is delayed a few days in the group comprising the more efficacious treatments, or, in other words, that the relapses occur only a few days earlier after the smaller doses of quinine than they do after the larger doses. This being so, we can ignore the fact that the cases in each of the twenty-one series were treated in a different way, and can group together all the four hundred and five cases comprising the twenty-one series and consider the time incidence of all the two hundred and sixty-eight relapses which were observed.

TABLE V.

Showing the percentage of the total relapses observed which occurred during each 3-day period.

Observation period after cessation of treatment in 3-day periods	Number of relapses in each 3-day period	Percentage of total relapses (268) in each 3-day period
1-3	7	2.61
4-6	12	4.48
7-9	34	12.68
10-12	58	21.64
13-15	63	23.50
16-18	34	12.68
19-21	21	7.83
22-24	12	4.48
25-27	8	2.98
28-30	3	1.12
31-33	6	2.23
34-36	2	0.74
37-39	4	1.49
40-42	0	0.00
43-45	0	0.00
46-48	1	0.37
49-51	0	0.00
52-54	0	0.00
55-57	2	0.74
58-60	1	0.37
Total	268	99.94

The time incidence of relapses can be considered in three ways:—

1. *In reference to the relapses themselves, i.e. the percentage of the total relapses which occurred during each period of time.*

Table V shows the number of relapses that occurred in each three-day period after the cessation of treatment and what percentage these numbers form of the total relapses. The percentage of relapses gradually rises from 2·61 in the one to three-day period to a maximum of 23·5 in the thirteen to fifteen-day period; after this it rapidly falls to the fifty-eighth day, subsequent to which no relapse was observed.* Grouping the incidence into fifteen-day periods, we find that 64·91 per cent. of relapses occurred in the first fifteen-day period, 29·09 in the second, 4·46 in the third, and 1·48 in the fourth (Table V and Chart II, graph 1).

2. *In reference to the total cases treated, i.e. the percentage of the total cases treated which relapse during each period of time.*

Table VI shows that the relapses increase from seven in the one to three-day period to a maximum of sixty-three in the thirteen to fifteen-day period, and subsequently decrease rapidly until, after the fifty-eight to sixty-day period, no further relapses were observed.*

The percentage of cases which relapsed during each three-day period is shown in the last column. As from time to time cases which had not relapsed were discharged from hospital, it is necessary in estimating the percentage of relapses in any given three-day period to deduct from the original total of four hundred and five such non-relapse cases as had been previously discharged. Thus in the period twenty-two to twenty-four days, twelve cases relapsed; in determining what percentage this is, it is necessary to deduct from the original total of cases (four hundred and five) the four who had not relapsed but who had left hospital prior to the twenty-second day, giving therefore twelve relapses out of four hundred and one cases (2·99 per cent.).

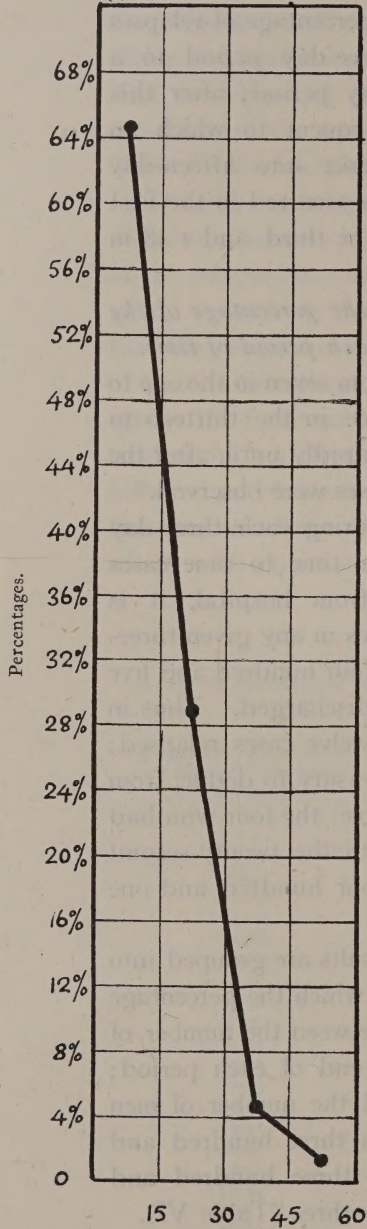
In Table VII and Chart II, graph 2, the results are grouped into fifteen-day periods. The number of cases on which the percentage of relapses is based is taken as the average between the number of men in hospital at the beginning and at the end of each period; thus in the thirty-one to forty-five-day period the number of men under observation on the thirty-first day was three hundred and ninety-seven and that on the forty-fifth day, three hundred and eighty-nine—average three hundred and ninety-three (Table VI).

* *Vide addendum.*

CHART II.

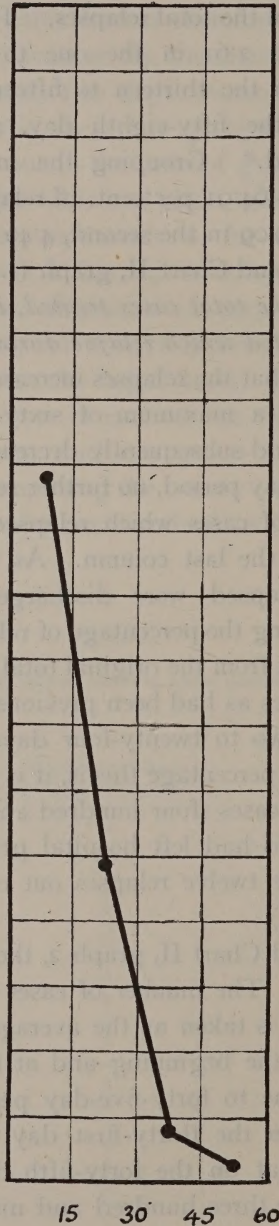
GRAPH 1.

Percentage of total relapses
in each 15-day period.



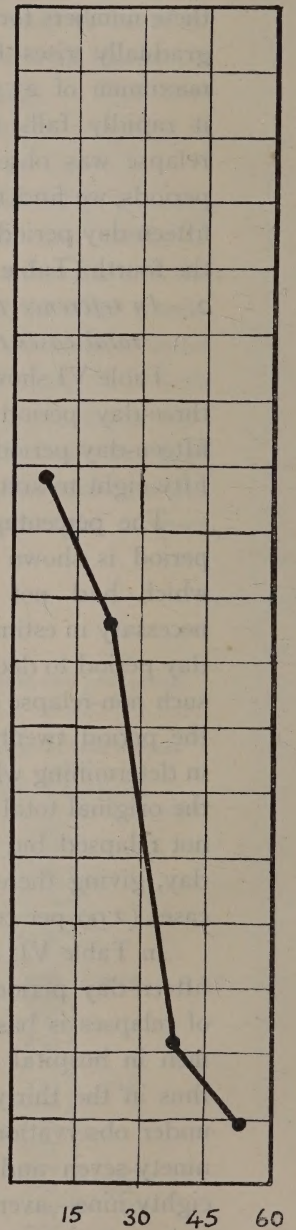
GRAPH 2.

Percentage of cases treated
which relapse in
each 15-day period.



GRAPH 3.

Percentage of cases treated not
having previously relapsed which
do so in each 15-day period.



Days after cessation of treatment.

TABLE VI.

Showing the percentage of cases treated which relapsed during each 3-day period after cessation of treatment.

Observation period after cessation of treatment in 3-day periods	Number of cases treated on which the percentage of relapses is calculated*	Number of non-relapse cases still in hospital at beginning of each 3-day period	Number of cases which relapse during each 3-day period	Percentage of cases treated which relapse during each 3-day period
1-3	405	405	7	1.73
4-6	405	398	12	2.96
7-9	405	386	35	8.64
10-12	404	350	57	14.11
13-15	403	292	63	15.63
16-18	403	229	34	8.44
19-21	402	194	21	5.22
22-24	401	172	12	2.99
25-27	401	160	8	2.00
28-30	399	150	3	0.75
31-33	397	145	6	1.51
34-36	392	134	2	0.50
37-39	391	131	4	1.02
40-42	391	127	0	0.00
43-45	389	125	0	0.00
46-48	386	122	1	0.26
49-51	383	118	0	0.00
52-54	380	115	0	0.00
55-57	377	112	2	0.53
58-60	376	109	1	0.26
61-63	353	85	0	0.00
64-66	332	64	0	0.00
67-69	313	45	0	0.00
70-72	309	41	0	0.00
73-75	303	35	0	0.00
76-78	295	27	0	0.00
79-81	290	22	0	0.00
82-84	285	17	0	0.00
85-87	283	15	0	0.00
88-90	281	13†	0	0.00

* *i.e.*—The original number of cases (405), less those non-relapse cases who have left hospital previous to the *beginning* of each 3-day period.

** This number represents an average between two figures: (1) the total number of cases treated, less those non-relapse cases who left hospital previous to the beginning of a 15-day period; and (2) this figure less the number of non-relapse cases discharged during that period.

*** The bracketed figures represent the number of non-relapse cases discharged from hospital during the various 15-day periods.

† None of these thirteen cases relapsed in observation periods of 90, 91, 92, 93, 99, 100, 101, 102, 103, 108, 140, 164, and 165 days respectively.

The results show that of four hundred and five cases treated, approximately 43 per cent. relapse during the first fifteen days after cessation of treatment, 19·5 per cent. during the second fifteen-day period, 3 per cent. during the third, 1 per cent. during the fourth and none during the fifth and sixth fifteen-day periods or later.* These figures are not absolutely correct, because, as already explained, certain cases which had not relapsed left hospital before the observation period was complete, but as the number of these is small up to the fifty-eighth day, which was the last occasion* on which a relapse was observed, the error only affects the decimal.

TABLE VII.

Showing the percentage of cases treated which relapsed during each 15-day period after cessation of treatment.

Observation period after cessation of treatment in 15-day period	Number of cases treated on which the percentage of relapses is calculated†	Number of cases which relapsed during each 15-day period	Percentage of cases treated which relapsed during each 15-day period
1-15	404	174	43·07
16-30	401	78	19·45
31-45	393	12	3·05
46-60	381	4	1·04
61-75	328	0	0·00
76-90	288	0	0·00
91-105	276	0	0·00
106-120	271	0	0·00
121-135	271	0	0·00
136-150	270	0	0·00
151-165	270	0	0·00

* *Vide* addendum.

† *Vide* Table VI.

3. *In reference to remainders after deducting from the original total of cases treated those cases which have relapsed, i.e. the percentage of those who not having relapsed at the beginning of each period of time, do so during the period.*

From Table VIII and Chart II, graph 3, it will be seen that in the first fifteen-day period one hundred and seventy-four relapses occurred among four hundred and four cases (the average number of cases under observation during the period—four hundred and five at the beginning and four hundred and three at the end (Table VI)); this gives a percentage of relapses of 43. In the second fifteen-day period, seventy-eight relapses occurred among the remaining two hundred and twenty-seven who had not relapsed during the first fifteen-day period (two hundred and twenty-seven being the average between two hundred and twenty-nine in hospital at the beginning of the period and two hundred and twenty-five at the end, four cases having left hospital during the period (Table VI); this gives a percentage of relapses of 34.3. The percentages of relapses amongst the cases not having previously relapsed are similarly calculated for the remaining four fifteen-day periods.

TABLE VIII.

Showing what percentage of cases not having previously relapsed did so in any 15-day period.

Observation period after cessation of treatment in 15-day periods	Average number of cases in hospital which have not relapsed in each 15-day period	Number of relapses in each 15-day period	Number of relapses expressed as percentages of the non-relapse cases under observation in each 15-day period
1-15	404	174	43.0
16-30	227	78	34.3
31-45	141	12	8.5
46-60	117	4	3.4
61-75	60	0	0.00
76-90	20	0	0.00
91-105	8	0	0.00
106-120	3	0	0.00
121-135	3	0	0.00
136-150	2	0	0.00
151-165	2	0	0.00

The data as presented in Table VIII are best adapted for furnishing an answer to the problem stated at the commencement of this paper, namely, what is the shortest observation period after which a man who has not relapsed can be discharged from hospital, with but a small risk of subsequent relapse?

Table VIII shows that 43 per cent. of cases relapsed during the first fifteen days after cessation of treatment, and that 34·3 per cent. of the remainder relapsed during the next fifteen days. Only a small percentage of those who had not then relapsed did so during each of the next two fifteen-day periods, whilst in the fifth and sixth fifteen-day periods, or later, no relapses occurred. Consequently, if a man has not relapsed for fifteen days after treatment, his chance of relapsing during the next fifteen days is 34 per cent.; but if he has not relapsed for thirty days, his chance of relapsing during the following fifteen days is only 8·5 per cent., whilst if he has not relapsed for forty-five days, his chance is reduced to 3·4 per cent. during the following fifteen-day period.

The number of cases observed for periods over sixty days was an average of sixty for sixty-one to seventy-five days, twenty for seventy-six to ninety days, and thirteen for periods varying from ninety-one to one hundred and sixty-five days. No relapses were observed later than the fifty-eighth day.* Moreover, as the percentage of relapses falls so rapidly from the first to the fourth fifteen-day period, we may logically infer that only a very small proportion of those cases who have not relapsed during an observation period of sixty days will do so subsequently. This inference can only be regarded as probable, because we do not know what may happen to these cases if subjected to a different set of conditions to those under which we made our observations, viz., those of hospital patients going out daily. It may be urged also that the inference is incorrect, for it is known that cases do relapse at long intervals. We may point out, however:—(1) That we know of no series of published cases *that has been observed for sixty days or longer after treatment, and in addition has been controlled by daily blood examinations*. It is quite possible, for example, that some relapses at long intervals may represent cases which after treatment show parasites without clinical symptoms. Such cases would have been eliminated by daily blood examinations subsequent

* *Vide addendum.*

to treatment, and would not thus come into the category of late relapses. We propose to deal with this question in a future study. (2) Accepting relapses at long intervals as an established fact, we have no data to show what percentage they form of any definite series of cases treated. We would add that we are fully aware of Caccini's (1902) papers on relapses, but his data as presented are to us unintelligible.

The general conclusion to be drawn from these observations appears to be that if a case of simple tertian malaria has not relapsed parasitically within four weeks of cessation of treatment he can be discharged from hospital with a risk of relapse of only about 13 per cent., whilst if he has not relapsed within six weeks of cessation of treatment his risk of subsequent relapse is reduced to less than 5 per cent.

It must again be emphasised that the conclusions are based on the fact that frequent (in most cases daily) blood examinations were made, and consequently when we refer to a case as not having relapsed for six weeks, we mean that frequent (almost daily) examinations of his blood during that period were negative.

REFERENCE

CACCINI, A. (1902). *Journ. Trop. Med. & Hyg.*, Vol. V, p. 119 *et seq.*

ADDENDUM (13.4.18)

Since writing this paper, two of the cases considered who had not relapsed in sixty-six and ninety-one days respectively, did so on the one hundred and third and one hundred and twenty-seventh days.



